

JAPANESE MEDICAL MATERIAL

B-190

BLINOLIN; BOROTOPIN; TRIBORATIN; BOROVERTIN

(Methenamine Tri-meta-borate)

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MEDICAL ANALYSIS SECTION

5250th Technical Intelligence Company
APO 500

BLNOLIN; BOROTOPIN; TRIBORATIN; BOROVERTIN

(Methenamine Tri-meta-borate)

SOURCE: Tokyo, Japan.

IMPORTANCE: Not previously reported. All of these preparations are claimed to be effective as urinary antiseptics even in alkaline urine. No identical methenamine salts are listed in available standard American references.

DESCRIPTION: Methenamine Tri-meta-borate is available under the following proprietary names:

1. Blenolin
2. Borotopin
3. Triboratin
4. Borovertin

All are white fine powders contained in glass bottles and generally further packaged in a cardboard container.

Each has a slight but characteristic odor.

SUMMARY OF GENERAL INFORMATION: Chemically, all of these products are claimed to be methenamine tri-meta-borate, $(CH_2)_6N_4 \cdot 3HBO_2$. They are available in the following forms and sizes:

	<u>Blenolin</u>	<u>Borotopin</u>	<u>Triboratin</u>	<u>Borovertin</u>
Powder	25 gm	25 gm	25 gm	25 gm
	100 gm	100 gm	100 gm	
		250 gm	250 gm	
		500 gm	500 gm	

Blenolin is also marketed in bottles containing 50 and 100 tablets.

An official preparation, Uroboramine, is listed in the supplement to the Pharmacopoeia Japonica V. The book, "Facts on Current Pharmaceuticals", compiled by Chuzo Hata, Mamoru Zukawa and Hiroo Takeishi, also records that "Nichiborin" is the Japan Pharmaceutical Company's trade-marked name for their product.

Translations of the literature enclosed with Borotopin, Triboratin and Blenolin are a part of this report and include the chemistry, pharmacological action, indications, references, routes of administration, dosage, cautions and manufacturers.

Mr. C. Hata, during interrogation, stated that methenamine tri-meta-borate may be produced as follows:

Triturate one mole of methenamine with three moles of boric acid in the presence of some alcohol. Dehydrate the resulting liquid on a water bath until a powder results.

Although these products are not listed in available standard American references, the principle involved, that of combining methenamine with an acid-forming salt, has long been employed.

It is claimed that formaldehyde is liberated in either acid or alkaline urine. Although the claim is thus made that methenamine tri-meta-borate is active even in alkaline urine,

substantiating experimental evidence is not presented.

Inasmuch as boric acid has not been commonly accepted, for internal use by American physicians, and the sulfonamides have largely replaced methenamine in the treatment of urinary infections, only limited use is to be expected of these preparations. They may be indicated in resistant urinary infections where it is highly desirable to change from one drug to another in order that the bacteria do not become markedly resistant to a specific medicament.

PHOTOGRAPHS:

Figure 1 - Packages as received:

Blenolin

Borotopin

Triboratin

Borovertin

Figure 2 - Medicinal containers

As above

Figure 3 - Blenolin literature

Figure 4 - Borotopin literature

Figure 5 - Triboratin literature



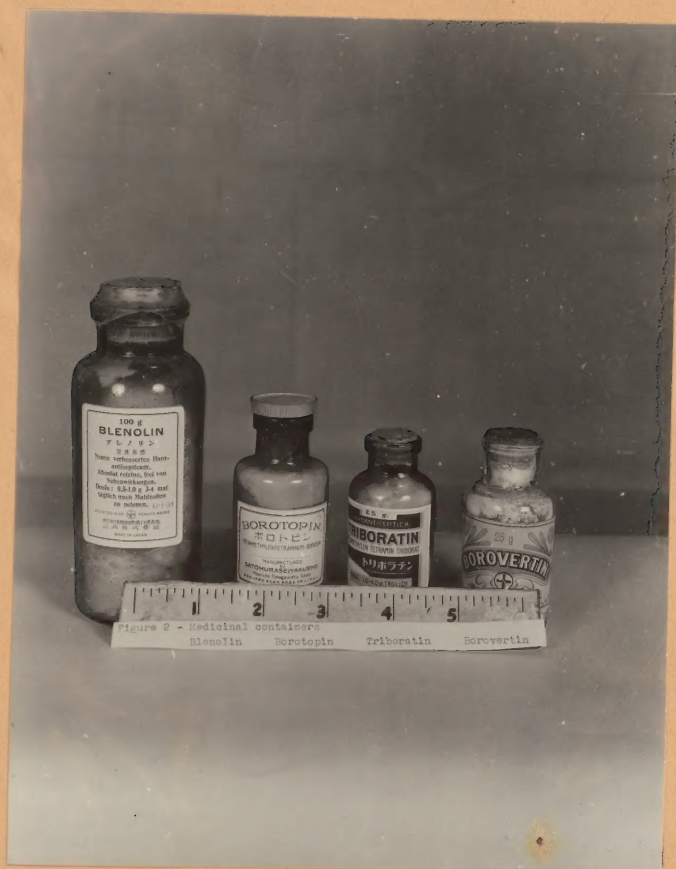


Figure 2 - Medicinal containers
Blenolin Borotopin Triboratin Borcvertin

淋疾内服新薬

ブレノリン BLENOLIN

粉末及錠劑

本品はドクトル松本需一郎先生の考案創製せられたる所にして、氏は從來世に用ひらるゝバルサム劑の胃腸を害し、腎臓を刺戟し、乃至皮膚を侵す等の副作用あるを慨し、又彼のホルムアルデヒド劑の体内分解遅徐にして急性淋の疼痛及利尿困難を救ふの能なきを思ひ、即ち彼の副作用を除き是の缺點を補ひ、兩者の長所を取りて此ブレノリンを創製せられたり。

本品はヘキサメチレンテトラミンと硼酸とを結合せしめたる一新化合物にして、從來のホルムアルデヒド劑と其撰を異にし、体内の分解敏速にして之を動物試験に徴するに、僅に三十分時にして既に尿中出现す。又本品は毫も消化器を害することなく腎臓及皮膚等に於けるバルサム劑の副作用を見ること無し。

而して本品の效驗の著明なること從來の治淋薬に嘗て見ざる所なり。乃ち急性症に在りては服用後尿量増加し五日乃至一週日にして膿汁の分泌減少するを目撃し、慢性病の再燃性尿道炎に在りては二、三日にして疼痛及尿意頻數消失す。

又膀胱炎を發したる者の如きは、服用第二日に於て既に尿に酸性反應を呈し、患者の苦痛倏忽にして去る。

本品は一回〇・五瓦錠劑は二錠、宛一日三回服用するを普通とす。患者は本品服用と共にアルコール飲料及其他の刺激性食物の攝取を嚴禁し、房事を避くる等の攝生を爲すべし。

本品の効力の偉大なるは創製者松本ドクトルが一百有餘人の淋毒性諸症に對し行はれたる實驗に徴して明かなる所なるも、尙次に一、二大家の實驗報告を抄録して證左と爲す。

醫學博士櫻根孝之進先生、(前略) 用量は一日六錠乃至十二錠を用ひ長きは既に八週間以上持長せるも胃の症狀を訴へたるもの無し、其他副作用と認むべきものなかりき。以上の如く、殊に急性尿道炎淋に於ては内服薬として應用の價值あるべく、殊に輕便にして服用し易く且つ副作用の少きは本劑の特點なるべくと存候。

醫學博士緒方正清先生、松本氏製劑ブレノリンは副作用なき利尿殺菌劑として有效のものなることを證す。

醫學博士宇野朗先生、(前略) 本劑は他の治淋劑の如く胃腸を障礙することなきは内服劑として甚だ推奨するに足るものと信ず。バルサム製劑の如き、サリチル酸製劑の如き、皆悉く多少胃腸を害せざるはなし。故に長時間持續し難きの失あり。

之に反して本劑の其弊なきは確に他薬に異る優良の點とす(下略)。

用法及用量

一回量 (粉末 〇・五乃至一・〇瓦
錠劑 二錠乃至四錠 (一錠 〇・二五瓦))
一日量 (粉末 一・五乃至四・〇瓦 三回乃至四回分服
錠劑 六錠乃至十六錠 三回乃至四回分服)

本品はバルサム劑の如く不快なる臭味を有せざるを以て患者の嫌厭を來すことなく、服用容易なり。用時は食後とす。

病症の輕重に依り増量して用ふるも何等の副作用を伴ふことなし。

包裝 粉末 二五瓦入、一〇〇瓦入
錠劑 五〇錠入、一〇〇錠入

發賣元

三共株式會社

本社 東京市日本橋區室町二丁目

支店 大阪市東區道修町一丁目

出張所 臺北市表町一丁目

振替口座 臺灣二四六二番

(L.F.E.)

無刺激性尿路消炎殺菌劑 (内服用)

ボロトピン BOROTOPIN.

Hexamethylentetraminum Boricum.

細菌に由来する尿路疾患の治療に當り、ウロトロピンの効果に就ては、既に醫學界に於て確認せられたる所なり。然して、ウロトロピンが、酸性尿中に於てのみ強力なる作用を發するのみ、アルカリ性又は中性尿中に於ては殆んど無効なるのみ、又は作用微弱なる事も、亦周知の事實なり。茲に於てウロトロピンの、斯の如き藥理的欠点を補ふべく、幾多研究の結果、完成せられたる物は、即ち三縮酸ウロトロピンにして、この物は、アルカリ性尿中に於ても、同強力なる殺菌性を發揮し、ウロトロピンよりも一層迅速なる効果を顯し、即ち醫藥の實用する所となるに至れり。

ボロトピンは、即ち三縮酸ウロトロピンと、其化學的集積を同じくするものにして、周知なる化學的操作のもとに製造せられ、其品質に於て、内外幾多類似品に比し、其適を異にし、今や國産品として代表的製品と認められ、醫界に推奨せらるゝに至れり。

即ち本品は前日本藥局方に幾多の類似品を投擲して、只獨り本品のみ收斂せらるゝの光榮は蓋し其品質の優秀なるを立證せられたるものなるべし。

【化學的性狀】

本品は $(C_6H_{12})_4N_4 \cdot 3H_2BO_3 \cdot 3H_2O$ (Hexamethylentetramin triborat) の集積にして略々苦鹹を味する無臭白色の微細なる結晶性粉末なり、エーテルには不溶なるも十一分の水及び五〇分のアルコールに溶解す、而して其水溶液は透明にして弱酸性の反應を呈す。

【藥理的特長】

- 1、本品は尿の性狀の如何に關せず、酸性尿又はアルカリ性尿中に於てもよくホルムアルデヒドを產生するは従来の單なるウロトロピンに優る特長なり。
- 1、本品は尿路の疾患の原因たる、球菌屬及桿菌屬に對し殺菌力強く、從つて、細菌狀淋菌、淋菌、並に大腸菌及びチフス菌等の發育を停止せしめ、且つ之等の殺菌作用を發揮す。
- 1、本品は、純粹なる化學的集積品にして、濃縮性なく、且つ他のアルカリ性劑例へば重曹との配合薬品を考慮することなく、内服容易にして、之を持續的に用ゆるも何等胃腸刺激を起すことなきは勿論、他の有害なる副作用を見ることなし。
- 1、本品の内服に依り、排尿時の不快、疼痛又は尿意頻數を停退せしめ、併かも尿路の細菌性發熱は數日多量の解熱劑を要せずして下癒するは本品の殺菌作用にして、次で排泄せる尿が漸次透明となるは、更に本品の藥効的經過を証明するものなり。

【適應症】

○男女急性慢性膀胱炎

(淋菌性、結核性、大腸菌性)

○急性腎盂炎

○チフス菌尿路の消毒

○泌尿科疾患併發性症の預防

急性扁桃體炎、猩紅熱、麻疹、インフルエンザ等、是等の疾病の經過中膀胱炎並に腎臟炎の預防として忘るゝべからざる良劑なり。

【用法及用量】

大人一日量一・〇乃至五・〇瓦(一回量〇・五瓦)

主として水劑とするも場合によつては散劑として用ゆるを防げず。

本品使用に際し適宜の利尿劑を併用すれば病勢の經過を良好ならしむるものなり。

【包裝】

粉末 二五瓦 一〇〇瓦 二五〇瓦 五〇〇瓦

製造所 里村製藥所
東京市深川區毛利町
電話本所 〇九九六番
發賣元 合株式里村商店
東京市日本橋區本町三丁目
電話日本橋 三三〇七 〇〇
三三〇七 〇〇

内服尿路殺菌剤

トリボラチン

TRIBORATIN

— 集 成 —

トリボラチンは $(\text{CH}_2)_6\text{N}_4 \cdot 3\text{HBO}_3$ (Hexamethylenetetramin triborat) なる集成を有す。

— 特 長 —

トリボラチンは白色の粉末にして苦鹹味を有し11分の水並に50分のアルコールに溶解しエーテルには不溶解なり、其の水溶液は弱酸性の反應を徴す、本剤は藥學的純品にして濕潤性なく服用極めて容易なり。

— 作 用 —

本剤の作用はヘキサメチレンアトラミンによりて生ずる口腔及胃粘膜の刺戟その他の缺點を補ひその防腐作用を更に強大ならしめたるものにして體內に於て分解せるホルムアルデヒド及硼酸は共にその防腐作用を速に尿に及し毫も患部を刺戟する等の事なし而も其のホルムアルデヒドの析出作用は長時に亘りて持續し就中淋菌、大腸菌、チブス菌に對し強烈なる作用を呈することは細菌學的研究に依りて立證さるゝ處なり。本剤は又アルカリ尿の組織中に於てもよく奏効し服用後潤濁尿を速に透明となす。

— 適 應 症 —

膀胱加答兒、膀胱結核、腎盂炎、尿道炎、淋毒性膀胱疾患、細菌尿その他一般尿路の防腐及殺菌に應用さる。

— 用法及用量 —

普通内服用量は大人一回量 0.5g 一日量 1.0~2.0g を與ふ更に多量 (一日量 3~4.0g) を使用するも可なり。

本剤は單味又は他藥と混和散劑となすも良好にして又水劑となすにも適す。水劑にする場合ウワウルシ葉煎等と併用する事は最も良好なる結果を見るべし (但ウワウルシ葉煎と併用の場合は多少潤濁する事あるも効力に變化なし)

— 處 方 例 —

處 方	トリボラチン	1.5	處 方	ウワウルシ葉煎 (8.0)	90.0
	乳 糖	1.0		トリボラチン	1.5
	右一日三回分服			シ ロ ッ プ	10.0
				右一日三回分服	

— 包 裝 —

25瓦入	¥	.60	100瓦入	¥	2.20
250瓦入	¥	5.00	500瓦入	¥	9.00

御注意 類似名のものがあります。岩城トリボラチンと御指定願ひます。

製 造 所 東京市品川区東大崎 合 資 會 社 岩 城 製 藥 所

TRANSLATION OF THE LITERATURE ENCLOSED WITH BLENOLIN

New Internal remedy for Gonorrhea

BLENOLIN

Powder and Tablets

This drug was synthesized and manufactured under the supervision of Dr. Jutchiro Matsumoto. Balsam drugs are irritants to the skin, kidney, stomach and intestines. Methenamine acts too slowly to relieve acute gonorrhea and painful urination. These difficulties were overcome and this new drug was synthesized by Dr. Matsumoto.

This new compound differs from methenamine in being methenamine with boric acid. It dissolves very quickly in the body. In animal tests it was detected in the urine thirty minutes after administration. This drug is not irritant to the kidneys and skin nor does it injure the digestive organs like the balsam drugs. We have never seen such an effective drug. In acute infections, the amount of urine will increase and the discharge will decrease day by day. Sometimes five to seven days will be required. In chronic urethritis, relief will come in two to three days. In bladder inflammation, this drug will cause the urine to become acid and relief will follow.

Dosage: One-half gram (or two tablets) three times a day. The patient must refrain from alcoholic beverages, irritant foods and sexual intercourse. The success which Dr. Matsumoto obtained in over 100 cases of gonorrhea proves its effectiveness.

Several great physicians report the following:

Konoshin Sakurane (Doctor of Medicine)

From 6 - 12 tablets per day were given to patients for as long as eight weeks without deleterious effects.

Masakiyo Ogata (Doctor of Medicine)

I certify that Blenolin is useful as a diuretic and disinfectant and does not have any untoward reactions on the body.

Ro Uno (Doctor of Medicine)

I recommend this drug over other gonorrheal cures as it is non-irritating to the digestive system. It is not injurious to the digestive organs like the balsams or salicylic acid. This drug can be used for long periods without harm.

Directions for use:

Individual (Powder 0.5 - 1.0 gm.)

Dose (Tablets 2 - 4 tablets (each tablet = 0.25 gm.))

Maximum (Powder - 1.5 to 4.0 gm.)

Daily dosage (Tablets - 6 to 16 tablets)

These amounts must be divided into three or four doses. This drug can be taken orally, inasmuch it does not possess any bad odor like the balsams. It should be taken after meals. No reaction will be noted even if larger doses are required in stubborn cases.

Packaging:

Powder	25 gm	100 gm
Tablet	50 tablets	100 tablets

Sold by:

Sankyo Co. Ltd.

TRANSLATION OF THE LITERATURE ENCLOSED WITH BOROTOPIN

Non irritant antiphlogistic and antiseptic for
the urinary tract (Internal Use)

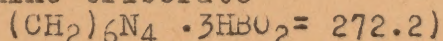
BOROTOPIN

Hexamethylenetetraminum Boricum

The effect of methenamine in the treatment of infections of the urinary passages has been proved in medical circles. It is also known that methenamine acts in acid urine, while its action in alkaline urine is very diminished. For this reason methenamine triborate which also shows remarkable antiseptic action in alkaline urine, was prepared.

This preparation shows better results than methenamine. Of all similar preparations in medicine, we have the honor of having our medicament included in the Quasi-pharmacopoeia Japonica. By this, you know the excellence of this medicine.

Chemical properties: Borotopin is a preparation of hexamethylenetetramine triborate



It is an odorless crystalline powder with a slightly bitter taste. It is soluble in alcohol and water but not in ether. It's solution is colorless and shows a weak acid reaction.

Pharmacological properties:

- (1) Borotopin produces formaldehyde equally well in acid or alkaline urine, a fact not true about methenamine.
- (2) Borotopin acts against the micrococci, colon bacteria, typhoid bacteria, etc.
- (3) Borotopin is a pure, dry chemical. It may be mixed with other alkaline medicaments (Sodium Bicarbonate) or taken alone for long periods, without ill effects.
- (4) By using Borotopin internally, painful frequent urinations are decreased. Because the fever of the urinary passages decreases, we know of its antiseptic action. Another proof of its action is the clear urine which results.

Indications:

- (1) Acute or chronic cystitis of both sexes
(Bacteria of gonorrhea, tuberculosis, large intestine)
- (2) Acute pyelitis
- (3) Typhoid bacteria in urinary passages
- (4) Prevention of complications of urinary infections. Borotopin is indispensable for prevention of pyelitis, and inflammation of the kidney in acute tonsillitis, scarlet fever, measles, influenza etc.

TRANSLATION OF THE LITERATURE ENCLOSED WITH TRIBORATIN

TRIBORATIN

Hexamethylenetetramin-triborat

Chemistry: Triboratin is hexamethylenetetramin-triborat,
 $(\text{CH}_2)_6\text{N}_4 \cdot 3\text{HBO}_3$

Characteristics: Triboratin is a white powder with a bitter and salty taste, soluble in water (11) alcohol (50) but not in ether. This preparation is pure, non-hygroscopic and can be easily taken by mouth.

Action: This drug was synthesized so as not to cause irritation of the oral cavity or the stomach and to increase the antiseptic action of methenamine. Its antiseptic action is due to its decomposition into formaldehyde and boric acid in the body without irritation to the affected part. This action continues for many hours, giving intense action against the gonorrhea coccus, typhoid bacillus and other intestinal bacillus. Bacteriological research proved this. The effectiveness of this drug in alkaline urine is proved by the fact that turbid urine becomes transparent.

Indications: Triboratin is indicated in catarrh of the bladder, tuberculosis of the bladder, pyelitis, urethritis, gonorrheal bladder, bacterial urine and other urinary diseases.

Directions for use: Adults: One to two grams per day in one-half gram doses. If necessary, three to four grams can be given. It can be given alone, with other powders or in solution. If a decoction of Uva-Ursi leaves is used as the solvent, better results can be obtained. Disregard turbidity in this solution.

Prescription Examples

Triboratin	1.5 gm	Decoction Uva Ursi (8.0)	90.0 gm
Lactose	1.0 gm	Triboratin	1.5 gm
Ft. Chart No.	3	Syrup	10.0 gm
Divide into 3 doses			

Packaging:

25 gm	¥ .60	100 gm	¥ 2.20
250 gm	¥ 5.00	500 gm	¥ 9.00

Caution: To avoid imitations, ask for Iwaki Triboratin.

Manufactured by:

Iwaki Pharmaceutical Co. Limited Partnership
Osaki, Shinagawa-Ku, Tokyo

Directions:

Adults: One to four (1 - 4) grams per day in doses of one half ($\frac{1}{2}$) gram. Although Borotopin is usually used in liquid preparations, the powder may also be administered. If a proper diuretic is used, better results will be obtained.

Packagings:

Powder - 25 gm., 100 gm., 250 gm., 500 gm.

Manufactured by:

Satomura Seiyakusho
Morimachi Fukagawaku Tokyo

Sold by:

Satomura Co. Ltd.
3 Chome, Honcho, Nihonbashi-Ku, Tokyo